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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/930,335	08/15/2001	Graham Paul Matthews	4-30811A/C1	1679

1095 7590 07/23/2002

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EXAMINER
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ART UNIT	PAPER NUMBER
1614	8

DATE MAILED: 07/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/930,335	MATTHEWS ET AL.	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *10,12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. This Office Action supercedes the Restriction Requirement mailed June 18, 02. According to the telephonic interview initiated by the applicant's representative, the instant application which is a continuation of PCT Patent Application No. PCT/EP00/01196, filed February 14, 2000 should have been subjected to US Restriction Rule 35 USC 121. Therefore, the examiner withdraws the previous Restriction Requirement according to PCT Rule 13.1.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121.

Group I, claim(s) 1-9, 11, drawn to a composition comprising N-benzoyl-staurosporine, a hydrophilic coponent and a surfactant, classified in class 540, subclass 545; class 424, subclass 450, 489, 499, 501, 502.

Group II, claim(s) 10 and 12-13, drawn to a method of use with said composition, classified in class514, subclass 211

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the process for using the product as claimed, for example the treatment of breast cancer, colon cancer, ovarian cancer, leukemia and multidrug resistance, can be practiced with another materially product (camptothecin analogs (US 5004758); triprolidine

(US 5114951); quinolyloxazole-2-ones (US 5190957); flavonoid compound (US 5336685), etc...).

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

3. If applicant elects Group (II) invention, it is subjected to further restriction as followings.

Group II-A, claim(s) 10, drawn to a method of treatment for treating subjects in need of N-benzoyl-staurosporine therapy with said composition.

Group II-B, claim(s) 12-13, drawn to a method of increasing bioavailability levels of N-benzoylstaruosporine with said composition.

Inventions II-A and II-B are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation and different functions.

Because these inventions are distinct for the reasons given above and the search required for Group II-A is not required for Group II-B, restriction for examination purposes as indicated is proper.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the

currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

5. During a telephone conversation with C. Wilus on July 12, 2002 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-9 and 11. Affirmation of this election must be made by applicant in replying to this Office action. Claims 10 and 12-13 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

6. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Priority

7. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(a)-(d) based upon an application filed in United Kingdom 9903547.9 on 02/16/1999. It is noted, however, that applicant has not filed a certified copy of the United Kingdom 9903547.9 application as required by 35 U.S.C. 119(b).

Specification

8. The instant specification refers to WO 94/09211 as the contents of which are incorporated by reference. However, the examination of that reference fails to support such claim. Applicant is requested to amend or delete the specification accordingly.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

9. Claim 1-2, 4-6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Weder et al. (US 5658898).

Weder'898 teaches or suggests a composition comprising N-benzoyl-staurosporine, a hydrophilic component (e.g., sorbitan, mannitol, glucose, lactose or fructose), purified lecithin from soybeans (e.g., LIPOIDS 100), a fatty acid tryglyceride (e.g., MIGLYOL 812) and polyoxyethylene sorbitan (e.g., TWEEN). See column 3, line 15 thru column 6, line 16; Claims 1-2.

In respective to claim 6, although the reference is silent regarding the claimed "HLB value", the referenced Tween and MIGLYOL 812 or soybean lecithin phospholipids, namely LIPOID S 100, must inherently possess the claimed properties and characteristics since the instant specification lists Tween as the "surfactant of high HLB value, e.g., HLB > 10" (page 5, line 28; page 7, lines 11-23) and MIGLYOL 812 or soya bean lecithins as the "surfactant having

a low HLB value, e.g., HLB <10" (page 8, line 4; page 8, lines 13-14; page 10, lines 4-5). Therefore, the reference clearly anticipates the claimed invention.

10. Claim 1-4 and 6 are rejected under 35 U.S.C. 102(e) as being anticipated by Weder et al. (US 5726164).

Weder'164 teaches or suggests a composition comprising N-benzoyl-staurosporin, a hydrophilic component (e.g., ethanol and water), polyoxyethylene/polyoxypropylene block copolymer (e.g., Pluronic F68 and Lutrol F68) and phospholipids, in paticular purified lecithin from soybeans (e.g., LIPOID S 100). See abstract and column 2, line 60 thru column 6, line 8.

In respective to claim 6, although the reference is silent regarding the claimed "HLB value", the referenced Pluronic F68 and soybean lecithin phospholipid, namely LIPOID S 100, must inherently possess the claimed properties and characteristics since the instant specification lists Pluronic F68 as the "surfactant of high HLB value, e.g., HLB > 10" (page 5, line 28; page 7, lines 28-31) and soya bean lecithins as the "surfactant having a low HLB value, e.g., HLB <10" (page 8, line 4 and page 10, lines 4-5). Therefore, the reference clearly anticipates the claimed invention.

It is noted to applicant that statement of intended use or purpose such as "for oral administration" or "intravenous administration" are not limiting to the interpretation of composition claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Weder et al. (US 5726164) in view of Henry et al. (US 5736542).

Dependent claim 7 further limits the parent claims, which are directed to a composition comprising N-benzoyl-staurosporine, a hydrophilic component and a surfactant, by "wherein the surfactant is selected from the group consisting of a polyoxyethylene castor oil, a polyoxyethylene alkyl ether, and a polysorbate, and the co-surfactant comprises a transesterified ethoxylated vegetable oil".

The teaching of Weder'164 has been discussed in above 35 USC 102(e) rejection.

Henry teaches or suggest the use of a transesterified ethoxylated vegetable oil (which is mixtures of mono, di and triglycerides and polyethelene glycol mono and diesters) in N-benzoylstaurosporine composition (column 1, line 44 thru column 2, line 9).

The teaching of Weder'164 differs from the claimed invention in the incorporation of a transesterified ethoxylated vegetable oil. To incorporate such teaching into the teaching of Weder'164, would have been obvious in view of Henry who teaches or suggests suggest the use of a transesterified ethoxylated vegetable oil in N-benzoylstaurosporine composition.

One having ordinary skill in the art would have been motivated to incorporate transesterified ethoxylated vegetable oil in N-benzoylstaurosporine composition such that the bioavailability of N-benzoylstaurosporine would be significantly increased.

12. Claims 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weder et al. (US 5726164).

Independent claim 9 reads on a composition comprising upto 20% by weight of N-benzoyl-staurosporine, 5 to 50% by weight of a hydrophilic component, 5 to 80% of a surfactant or surfactant mixture, 5 to 85% of a lipophilic component and 0.05 to 5% of an additive.

Independent claim 11 reads on composition comprising N-benzoylstaurosporine and having a variability of bioavailability levels of N-benzoylstaurosporine of from 5 to 17 %, an AUC of from 380 to 2000, or a Cmax of from 60 to 310, upon administration of a dose of N-benoylstaurosporine to fasted beagle dogs.

The teaching of Weder'164 differs from the claimed invention in (i) the specific amounts active and inactive ingredients (claim 9) and (ii) "AUC of from 380 to 2000", or "Cmax of from

60 to 310" (claim 11). However, optimization of amounts of known active and inactive ingredients in a composition is well considered within the skill of the artisan, and the artisan would be motivated to determine optimum amounts to get the maximum effect of the drug. Hence, the reference makes obvious the instant invention. Furthermore, the determination of AUC or Cmax having optimum therapeutic index is well within the level of one having ordinary skill in the art, absent evidence to the contrary.

Conclusion

13. No Claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703)308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon

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